

**AMENDMENT**

**IN THE CLAIMS:**

Please amend claims 21 and 38 pursuant to 37 C.F.R. §1.121 as follows (*see* the accompanying “marked up” version pursuant to 1.121):

1. (Unchanged) A method for detecting inactivation of a *CASP8* gene, comprising detecting a modification of genomic DNA comprising the *CASP8* gene, wherein such a modification results in inactivation of a *CASP8* gene.

2. (Unchanged) The method according to claim 1, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is detected by detecting the absence of a CASP8 protein in a sample from a cell.

3. (Unchanged) The method according to claim 2, wherein the absence of a CASP8 protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

4. (Unchanged) The method according to claim 1, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is methylation of *CASP8* promoter.

5. (Unchanged) The method according to claim 4, wherein methylation of the *CASP8* promoter is detected by methylation polymerase chain reaction (PCR) assay.

6. (Unchanged) The method according to claim 1, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is a mutation in the *CASP8* genomic gene.

7. (Unchanged) The method according to claim 6, wherein the mutation is selected from the group consisting of an insertion in the gene, a deletion of the gene, a truncation of the gene, a nonsense mutation, a frameshift mutation, a splice-site mutation, and a missense mutation.

8. (Unchanged) The method according to claim 6, wherein the mutation is a deletion in the *CASP8* gene.

9. (Unchanged) The method according to claim 8, wherein deletion of the *CASP8* gene is detected with a labeled nucleic acid probe.

10. (Unchanged) A method for diagnosis or prognosis of a cancer comprising detecting inactivation of a *CASP8* gene, wherein inactivation of the *CASP8* gene is indicative of the presence of a cancer or a poor prognosis.

11. (Unchanged) The method according to claim 10, wherein the cancer is a tumor in which a *myc* gene is amplified.

12. (Unchanged) The method according to claim 10, wherein the cancer is a neuroblastoma.

13. (Unchanged) The method according to claim 10, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is detected by detecting the absence of a CASP8 protein in a sample from a cell.

14. (Unchanged) The method according to claim 13, wherein the absence of a CASP8 protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

15. (Unchanged) The method according to claim 10, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is methylation of *CASP8* promoter.

16. (Unchanged) The method according to claim 15, wherein methylation of the *CASP8* promoter is detected by methylation polymerase chain reaction (PCR) assay.

17. (Unchanged) The method according to claim 10, wherein the modification of genomic DNA resulting in inactivation of a *CASP8* gene is a mutation in the *CASP8* genomic gene.

18. (Unchanged) The method according to claim 17, wherein the mutation is selected from the group consisting of an insertion in the gene, a deletion of the gene, a truncation of the gene, a nonsense mutation, a frameshift mutation, a splice-site mutation, and a missense mutation.

19. (Unchanged) The method according to claim 17, wherein the mutation is a deletion in the *CASP8* gene.

20. (Unchanged) The method according to claim 19, wherein deletion of the *CASP8* gene is detected with a labeled nucleic acid probe.

21. (Amended) A nucleic acid comprising at least a part of the genomic gene encoding *CASP8*, wherein the nucleic acid is selected from the group consisting of:

- a) a *CASP8* genomic DNA;
- b) a *CASP8* promoter;
- c) a nucleic acid amplified by primers that correspond to a sequence selected from the group consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13,

14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, and 28;

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- d) a ~~CASP8~~ exon;
  - e) a ~~CASP8~~ intron;
  - f) a nucleic acid having at least 15 bases and hybridizable under stringent conditions to a *CASP8* non-coding sequence.
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22. (Unchanged) The nucleic acid according to claim 21 which is a *CASP8* genomic DNA having a nucleic acid sequence as depicted in SEQ ID NO: 3, 4, 5, 6, 7, 8, 9, or 10.

23. (Unchanged) The nucleic acid according to claim 21 which is a *CASP8* promoter having a nucleic acid sequence as depicted in SEQ ID NO: 1 or 2.

24. (Unchanged) The nucleic acid according to claim 21 which is an oligonucleotide that hybridizes to the *CASP8* promoter, wherein the oligonucleotide is a PCR primer for the promoter.

25. (Unchanged) The nucleic acid according to claim 21 which is an oligonucleotide having at least 15 bases and hybridizable under stringent conditions to a *CASP8* non-coding

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sequence, which oligonucleotide is labeled.

26. (Unchanged) A kit for detecting inactivation of a *CASP8* gene comprising a detection assay for inactivation of a *CASP8* gene.

27. (Unchanged) The kit of claim 26, wherein the detection assay is an immunoassay.

28. (Unchanged) The kit of claim 26, wherein the detection assay comprises oligonucleotide PCR primers for amplification of at least a part of *CASP8* genomic DNA.

29. (Unchanged) The kit of claim 26, wherein the detection assay comprises a labeled oligonucleotide of at least 15 bases that specifically hybridizes to *CASP8* genomic DNA.

30. (Unchanged) A method of treating a cancer in a subject comprising administering an amount of a vector that expresses a gene encoding functional CASP8 effective to express a functional level of CASP8 into cells of the subject.

31. (Unchanged) The method according to claim 30, wherein the cancer is a tumor in which a *myc* gene is amplified.

32. (Unchanged) The method according to claim 30, wherein the cancer is a neuroblastoma.

33. (Unchanged) The method according to claim 30, wherein a *CASP8* gene is inactivated in tumor cells of the cancer.

34. (Unchanged) The method according to claim 30, wherein the vector comprises a promoter that provides for high level expression operatively associated with the gene encoding a functional CASP8, whereby the functional CASP8 is expressed at high levels.

35. (Unchanged) The method according to claim 30, wherein the vector is selected from the group consisting of a defective herpes virus (HSV) vector, a defective adenovirus vector, and a non-viral vector.

36. (Unchanged) A vector that expresses a gene encoding functional human CASP8

in human target cells.

37. (Unchanged) The vector of claim 36 comprising a promoter that provides for high level expression operatively associated with the gene encoding a functional CASP8, whereby the functional CASP8 is expressed at high levels.

*B2* 38. (Amended) A pharmaceutical composition for treating a cancer comprising the vector of claim 36 and a pharmaceutically acceptable carrier.

39. (Unchanged) A method of screening for a candidate compound that induces death-receptor-mediated apoptosis in cells where a *CASP8* gene is inactivated, comprising contacting cells in which a *CASP8* gene is inactivated with a candidate compound and detecting whether the cell undergoes apoptosis.

40. (Unchanged) The method according to claim 39, wherein the cell comprises a genetically modified death receptor of the Fas/TNFR receptor family operably associated with a reporter gene, whereby activation of the death receptor results in expression of the reporter gene.

41. (Unchanged) The method according to claim 40, wherein the death receptor is DR3.



42. (Unchanged) The method according to claim 40, wherein the reporter gene is a green fluorescent protein (GFP).

43. (Unchanged) The method according to claim 39, wherein inactivation of the *CASP8* gene results from methylation of *CASP8* promoter.

44. (Unchanged) The method according to claim 39, wherein inactivation of the *CASP8* gene results from a mutation in the *CASP8* genomic gene.

45. (Unchanged) A kit for screening for a candidate compound that induces death-receptor-mediated apoptosis in cells where a *CASP8* gene is inactivated, comprising cells in which a *CASP8* gene is inactivated and a detection assay for whether the cell undergoes apoptosis.

46. (Unchanged) The kit of claim 45, wherein inactivation of the *CASP8* gene results from methylation of *CASP8* promoter.

47. (Unchanged) The kit of claim 45, wherein inactivation of the *CASP8* gene results from a mutation in the *CASP8* genomic gene.